REMARKS

In the instant amendment, Claim 16 has been canceled, without prejudice, and Claims 12, 13 and 17-21 have been amended. After entry of the amendment, Claims 12, 13 and 17-21 are pending and under consideration.

I. AMENDMENTS

Amendments to the Specification. Paragraph 0011 of the substitute specification has been amended by including the full name and address of the depository used to deposit hybridoma lines producing monoclonals of the invention. Applicants submit this amendment does not add new matter, and entry thereof is respectfully requested.

Amendments to the Claims. Claim 12 has been amended to recite a kit for detecting an AAV antigen comprising a monoclonal antibody directed to an AAV type 2 capsid or a protein thereof in a suitable container. Support for this amendment is shown, for example, in the substitute specification in paragraphs 0011, 0015, 0016, 0023 and 0027.

Claims 13, and 18-21 have each been amended by the inserting "DSMZ," the current acronym used for DSMZ-Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (German Collection of Microorganisms and Cell Cultures), the depository in which the hybridomas producing the recited monoclonal antibodies were deposited as stated in the specification as originally filed, for example, in paragraph 0011 of the substitute specification.

Claim 17 is amended to be an independent claim and it recites an isolated monoclonal antibody directed against an AAV type 2 capsid or a protein thereof. The amendment to Claim 17 is supported by the specification, for example, paragraph 033, and Claim 17 as originally filed.

Applicants submit that no new matter is introduced by the instant amendment. Therefore entry of the amendment is kindly requested.

II. OBJECTION TO THE SPECIFICATION

The Patent Office states that identifying information set forth in 37 C.F.R. § 1.809(d) should be added to the specification. With the instant amendment of the specification, Applicants submit that the specification fully complies with the provisions of 37 C.F.R. § 1.809(d), by stating the accession number and dates of the deposits, a description of the deposited material, and the full name and address of DSMZ, the German depository in which the hybridomas producing monoclonal antibodies of the present invention were deposited. Accordingly, Applicants respectfully request that the objection to the specification be withdrawn.

III. REJECTIONS

A. Rejection of Claims 16 and 17 Under 35 U.S.C. § 101

Claims 16 and 17 stand rejected under 35 U.S.C. § 101 as allegedly encompassing nonstatutory products of nature. Claim 16 has been canceled, without prejudice, mooting the rejection with regard to that claim. Therefore, Applicants respectfully request the withdrawal of the rejection of Claim 16 under 35 U.S.C. § 101.

With regard to Claim 17, Applicants submit that the rejection is obviated since the instant amendment adds the word "isolated" into Claim 17 to exclude antibodies existing in nature, as suggested by the Patent Office. Therefore, withdrawal of the rejection of Claim 17 under 35 U.S.C. § 101 is respectfully requested.

B. Rejection of Claims 12, 13, and 18-21 Under 35 U.S.C. § 112, First Paragraph

Claims 12, 13, and 18-21 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabled.

Rejection of Claims 13 and 18-21. Claims 13 and 18-21 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Specifically, the Patent Office notes that there is no deposit statement stating the terms of the deposit or the extent of public availability in connection with the previously made deposits of hybridomas producing the monoclonal antibodies recited in Claims 13 and 18-21. The rejection of Claims 13 and 18-21 under 35 U.S.C. § 112, first paragraph, is obviated in view of the accompanying declaration from Dr. Jürgen Kleinschmidt, co-inventor of the subject matter of the instant application. *See* Declaration of Dr. Kleinschmidt dated August 28, 2003 (EXHIBIT 1).

In his declaration, Dr. Kleinschmidt states that the deposit was made under terms of the Budapest treaty and the extent of public availability, which, Applicants submit, satisfies the deposit requirements. The specification has been amended to reflect the deposit and the address of the depository.

In view of the above, Applicants respectfully request the withdrawal of the rejection of amended Claims 13 and 18-21 under 35 U.S.C. § 112, first paragraph.

Rejection of Claims 12 and 13. Claims 12 and 13 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly being non-enabled because undue experimentation would be required to use the kit in the manner required by the claims. The Patent Office contends that neither working examples of detecting AAV antigen in spontaneous abortion material are presented in the specification, nor teachings regarding the quantity of AAV antigen in spontaneous abortion material or specificity of the antibodies when presented in a complex mixture of biological materials. For reasons explained below, Applicants traverse the rejection of Claims 12 and 13 under 35 U.S.C. § 112, first paragraph.

As stated in the last sentence of paragraph 0041, the previously unknown concentrations of AAV in tissue culture supernatants, which to Applicants' knowledge comprise complex mixtures of biological materials, were determined using the immunoassay method described in the specification at paragraphs 0039-0041 by comparing the optical density obtained to the standard curve. As acknowledged by the Patent Office, the standard curve was generated using purified materials, and the A20 antibody was able to detect dilutions as little as 10 capsids/ml of AAV capsid. Thus, not only does the specification teach an immunoassay for detecting AAV, as acknowledged by the Patent Office, but the specification also states that AAV capsid in biological samples can be detected using the antibodies of the invention.

Moreover, the specification at paragraph 0033 teaches the production of four lines of hybridomas producing monoclonal antibodies. Each monoclonal has been characterized in terms of its AAV epitope and binding characteristics, *i.e.*, preferable conformational forms of AAV such as monomeric or oligomeric forms. *See* Table 1. The suitability of a particular monoclonal antibody for a particular use in detecting AAV antigen, *e.g.*, western blotting, immunoprecipitation or immunofluorescence, all standard techniques known to one of skill in the immunological arts., are detailed in Table 1. There is no reason to think that AAV type 2 capsid, regardless of biological source from which the capsid was obtained, would not be similarly detected using a technique appropriate for the particular antibody used in an assay.

For the above reasons, Applicants respectfully request that the rejection of Claims 12 and 13 under 35 U.S.C. § 112, first paragraph, be withdrawn.

C. Rejection of the Claims Under 35 U.S.C. § 102

1. The Rejection of Claims 16 and 17 Under 35 U.S.C. § 102(a)

Claims 16 and 17 are rejected under 35 U.S.C. § 102(a), allegedly as being anticipated by Ruffing *et al.* ("Ruffing"). Claim 16 has been canceled, without prejudice, thereby mooting the rejection. With regard to Claim 17, the rejection is respectfully traversed.

Where the applicant is one of the co-authors of a publication cited against his application, the publication may be removed if it is established that the relevant portions of the publication originated with, or were obtained from, the applicant. *See, e.g.*, 37 C.F.R. § 1.132; *Ex parte Hirschler*, 110 U.S.P.Q. 384 (Bd. App. 1952); *In re Katz*, 687 F.2d 450, 215 U.S.P.Q. 14 (CCPA 1982); MPEP § 2132.01. Attached as EXHIBIT 2, is the Second Declaration of Dr. Jürgen Kleinschmidt establishing that the production of anti-sera against AAV type 2 VP3 capsid protein, as described on page 6924, col. 1, of Ruffing, was originally conceived by Dr. Jürgen Kleinschmidt and produced by Michael Ruffing at the direction of Dr. Jürgen Kleinschmidt. Applicants submit that this affidavit establishes that the subject matter of anti-AAV antisera originated with Dr. Jürgen Kleinschmidt, and accordingly, Ruffing does not qualify as prior art under 35 U.S.C. § 102(a).

Moreover, Ruffing teach production of rabbit anti-sera, *i.e.*, polyclonal antibodies, directed to VP3 capsid protein (p. 6924, col. 1), but do not teach an isolated monoclonal antibody. Claim 17 recites an isolated monoclonal antibody. Thus, Applicants submit even if Ruffing were properly considered prior art under U.S.C. § 102(a), the cited reference would not anticipate Claim 17.

For reasons stated above, Ruffing does not qualify as prior art under 35 U.S.C. § 102(a), nor does it teach the limitations recited in Claim 17, and therefore Applicants respectfully request that the rejection of Claim 17 under 35 U.S.C. § 102(a) be withdrawn.

2. Rejection of Claims 16 and 17 Under 35 U.S.C. § 102(b)

Claims 16 and 17 are rejected under 35 U.S.C. § 112(b), allegedly as being anticipated by Hunter *et al.*, 1992, *J. Virology* 66:317-324 ("Hunter"), Georg-Fries *et al.*, 1984, *Virology* 134:64-71 ("Georg-Fries"), or by Hoggan *et al.*, 1966, *Proc. Natl. Acad. Sci. USA* 55:1467-1474 ("Hoggan"). Claim 16 has been canceled, without prejudice, thereby mooting the rejection. With regard to Claim 17, the rejection is respectfully traversed.

For a prior art reference to anticipate in terms of 35 U.S.C. § 102, every element of the claimed invention must be identically shown in a single reference. *See In re Bond,* 15 U.S.P.Q.2d 1566, 1567 (Fed. Cir. 1990).

The present invention is directed to an isolated monoclonal antibody directed against an AAV type 2 capsid, or a protein thereof, and a kit comprising the same. Applicants respectfully submit that neither of the cited references teaches each and every element of the claimed invention.

The Rejection Over Hunter. Hunter teach monoclonal antibodies directed towards AAV Rep protein and guinea pig anti-capsid anti-AAV serum (*i.e.*, polyclonal antibodies) (*see, e.g.*, Figure 8). Applicants submit that Hunter do not teach an isolated monoclonal antibody directed against an AAV type 2 capsid or a protein thereof as recited in Claim 17. Thus, Applicants submit that claim 17 is not anticipated under 35 U.S.C. § 102(b) by Hunter.

The Rejection Over Georg-Fries. Georg-Fries teach use of human anti-AAV anti-sera and of monoclonal antibodies directed specifically towards AAV-5 particles that bind to AAV type 5 structural proteins (*see, e.g.*, page 65, "Monoclonal Antibodies" and "Immunoprecipitation"). Applicants submit that Georg-Fries do not teach an isolated monoclonal antibody directed against an AAV type 2 capsid or a protein thereof as recited in amended Claim 17. Thus, Applicants submit that Claim 17 is not anticipated under 35 U.S.C. § 102(b) by Georg-Fries.

The Rejection Over Hoggan. Hoggan teach production of antisera against AAV types 1-3 (*i.e.*, polyclonal antibodies) (page 1468, "Preparation of antiserum"). Applicants submit that Hoggan do not teach an isolated monoclonal antibody directed against an AAV type 2 capsid or a protein thereof as recited in amended Claim 17. Thus, Applicants submit that Claim 17 is not anticipated under 35 U.S.C. § 102(b) by Hoggan.

For the reasons explained above, neither Hunter , nor Georg-Fries, nor Hoggan, anticipate Claim 17. Accordingly, Applicants respectfully request that the rejection of Claims 16 and 17 under 35 U.S.C. § 102(b) be withdrawn.

D. The Rejection of Under 35 U.S.C. § 103(a)

Claims 12, 13 and 18-21 are rejected under 35 U.S.C. § 103(a) for allegedly being obvious over several cited references.

1. Rejection of Claim 12

Claim 12 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Ruffing, or Hunter, or Georg-Fries. Applicants respectfully traverse this rejection.

Among the criteria for establishing *prima facie* obviousness under 35 U.S.C. § 103(a) is that all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 409 F.2d 981, 985, 180 U.S.P.Q. 580 (CCPA 1974); MPEP § 2143.03.

Claim 12 is directed to a kit for detecting an AAV antigen, comprising a monoclonal antibody directed to an AAV type 2 capsid or a protein thereof in a suitable container. Applicants respectfully submit that neither of the cited references teaches each and every element of the claimed invention.

The Rejection Over Ruffing. As explained in Section III.C.1., *supra*, Ruffing does not qualify as prior art under 35 U.S.C. § 102(a). Accordingly, Ruffing does not qualify as

prior art for use under a 35 U.S.C. § 103(a) rejection. *See, e.g., Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). Therefore, the rejection of Claim 12 under 35 U.S.C. § 103(a) over Ruffing is in error and should be withdrawn.

The Rejection Over Hunter. Hunter teach monoclonal antibodies directed towards AAV Rep protein and guinea pig anti-capsid anti-AAV serum (*i.e.*, polyclonal antibodies) (*see, e.g.*, Figure 8). Applicants submit that Hunter do not teach or suggest a kit comprising a monoclonal antibody directed against an AAV type 2 capsid or a protein thereof in a suitable container as recited in pending Claim 12. Thus, Applicants submit that Claim 12 is not rendered obvious under 35 U.S.C. § 103(a) over Hunter.

The Rejection Over Georg-Fries. Georg-Fries teach use of human anti-AAV anti-sera and of monoclonal antibodies directed specifically towards AAV-5 particles that bind to AAV type 5 structural proteins (*see, e.g.*, page 65, "Monoclonal Antibodies" and "Immunoprecipitation"). Applicants submit that Georg-Fries do not teach or suggest a kit comprising a monoclonal antibody directed against an AAV type 2 capsid or a protein thereof in a suitable container as recited in pending Claim 12. Thus, Applicants submit that Claim 12 is not obvious under 35 U.S.C. § 103(a) over Georg-Fries *et al.*

Accordingly, Applicants respectfully submit that the rejection of Claim 12 under 35 U.S.C. § 103(a) over Ruffing, or Hunter, or Georg-Fries should be withdrawn.

2. Rejection of Claims 13 and 18-21

Claims 13 and 18-21 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Georg-Fries and Ruffing. Applicants respectfully traverse the rejection.

The Rejection Over Ruffing. As explained in Section III.C.1., *supra,* Ruffing does not qualify as prior art under 35 U.S.C. § 102(a). Accordingly, Ruffing does not qualify as prior art for use under a 35 U.S.C. § 103(a) rejection. *See, e.g., Graham v. John Deere Co.*,

383 U.S. 1, 14 (1966). Therefore, the rejection of Claims13 and 18-21 under 35 U.S.C. § 103(a) over Ruffing is in error and should be withdrawn.

The Rejection Over Georg-Fries. Claim 13 recites a kit comprising one of the monoclonal antibodies of A1, A20, A69 and B1. Claims 18-21 are composition claims, each reciting one of the four monoclonal antibodies, *i.e.*, A1, A20, A69 or B1. Georg-Fries teach use of human anti-AAV anti-sera and of monoclonal antibodies directed specifically towards AAV-5 particles that bind to AAV type 5 structural proteins (*see, e.g.*, page 65, "Monoclonal Antibodies" and "Immunoprecipitation"). Applicants submit that Georg-Fries do not teach or suggest a monoclonal antibody directed against an AAV type 2 capsid or a protein thereof. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 13 and 18-21 under 35 U.S.C. § 103(a).

CONCLUSION

Applicants submit that Claims 12, 13, and 17-21 satisfy all the criteria for patentability. Therefore, Applicants respectfully request that the Examiner reconsider this application with a view towards allowance. The Examiner is invited to call the undersigned attorney if a telephone call could help resolve any remaining items.

No fee other than that for the Petition for a Three Month Extension of Time is believed to be due with this Amendment and Response. However, the Commissioner is authorized to charge all required fees or credit any overpayment to Pennie & Edmonds LLP U.S. Deposit Account No. 16-1150 (order no. 8484-013-999).

Respectfully submitted,

Date: October 7, 2003

Roger C. Rich 54,398

Roger C. Rich (Reg. No.)

For: Nikolaos C. George (Reg. No. 39,201)

PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090